A Phase I, single*center, double-blind, randomized, placebo-controlled, single and multiple ascending dose trial to evaluate the safety and pharmacokinetics of PTC857 in healthy volunteers.

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Primary ObjectivesPart 1 * Single Ascending DoseThe primary objective of the single ascending dose (SAD) part of the study is to characterize the safety and tolerability of a single dose of PTC857 in healthy subjects.Part 2 * Multiple Ascending...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Central nervous system infections and inflammations
Study type	Interventional

Summary

ID

NL-OMON49571

Source
ToetsingOnline

Brief title
CS0346-200065 PTC-857

Condition

- Central nervous system infections and inflammations

Synonym
Parkinson's Disease

Research involving

Human

Sponsors and support

Primary sponsor: PTC Therapeutics, Inc.
Source(s) of monetary or material Support: PTC Therapeutics Inc.

Intervention

Keyword: healthy volunteers, pharmacokinetics, safety, single and multiple ascending dose

Outcome measures

Primary outcome

Primary Endpoints:

Part 1 * Single Ascending Dose

The primary endpoint of the SAD part of the study is the overall safety profile characterized by type, frequency, severity, timing, and relationship to study treatment of any adverse events (AEs), vital signs, laboratory abnormalities, physical examination abnormalities, C-SSRS scores, or electrocardiogram (ECG) abnormalities.

Part 2 * Multiple Ascending Dose

The primary endpoint of the MAD part of the study is the overall safety profile characterized by type, frequency, severity, timing, and relationship to study treatment of any AEs, vital signs, laboratory abnormalities, physical examination abnormalities,

C-SSRS scores, or ECG abnormalities.

Part 3 * Food Effect

The primary endpoint of the FE part of the study is the food effect on PK parameters including area under the curve (AUC) from time zero to the last

quantifiable concentration (AUC0-t), maximum observed concentration (Cmax), and time corresponding to occurrence of Cmax (Tmax) after administration of a single dose of PTC857 in healthy subjects.

Secondary outcome

Secondary Endpoints:

Part 1 * Single Ascending Dose

The secondary endpoints of the SAD part of the study are:

PK parameters including AUC0-t, Cmax, Tmax, and dose normalized AUC (AUC0-t/D and AUC0-inf/D) and dose normalized Cmax (Cmax/D).

The PTC857 dose range for Part 2 (MAD) of the study.

Part 2 * Multiple Ascending Dose

The secondary endpoints of the MAD part of the study are:

PK parameters including AUC0-tau, Cmax, Tmax, tEHL, dose normalized AUC0-tau (AUC0-tau/D), Cmax/D, and the accumulation ratio based on AUC (Racc).

The PTC857 dose range and regimen for subsequent Phase 2 studies.

Part 3 * Food Effect

The secondary endpoint of the FE part of the study is any food effect on the safety and tolerability of a single dose of PTC857 in healthy subjects characterized by type, frequency, severity, timing, and relationship to study treatment of any AEs, vital signs, laboratory abnormalities, physical examination abnormalities, C-SSRS scores or ECG abnormalities.

Study description

Background summary

PTC857 is an orally bioavailable small molecule being developed by PTC Therapeutics, Inc. (PTC) for the treatment of neurological diseases characterized by high levels of oxidative stress and mitochondrial pathology, including Parkinson*s disease. PTC857 functions as an inhibitor of the oxidoreductase 15-lipoxygenase (15-LO) to reduce oxidative stress and spare reduced glutathione. Reduced glutathione is an essential intermediary metabolite that serves as the primary native cellular antioxidant and the cell*s primary defense against reactive oxygen species (ROS). In diseases characterized by high levels of oxidative stress, ROS production outstrips the available supply of glutathione resulting in depletion of glutathione and ROS-mediated cell injury and cell death. PTC857 inhibits 15-LO, the upregulation of which leads to a cascade of biological processes leading to a specific form of cell death termed ferroptosis. By inhibiting 15-LO, PTC857 is predicted to slow or prevent neurodegeneration in Parkinson's disease through the mechanism of action of inhibiting ferroptosis.

Study objective

Primary Objectives
Part 1 * Single Ascending Dose
The primary objective of the single ascending dose (SAD) part of the study is to characterize the safety and tolerability of a single dose of PTC857 in healthy subjects.
Part 2 * Multiple Ascending Dose
The primary objective of the multiple ascending dose (MAD) part of the study is to characterize the safety and tolerability of multiple doses of PTC857 in healthy subjects.
Part 3 * Food Effect
The primary objective of the food effect (FE) part of the study is to characterize the effect of food on the PK after administration of PTC857 in healthy subjects.

Secondary Objectives
Part 1 * Single Ascending Dose
The secondary objectives of the SAD part of the study are:
To characterize the single dose plasma PK profile of PTC857 in healthy subjects.
To determine a dose range for PTC857 that is appropriate for use in Part 2 (MAD) of the study.
Part 2 * Multiple Ascending Dose
The secondary objectives of the MAD part of the study are:
To characterize the multiple dose plasma PK profile of PTC857 in healthy subjects.
To determine a dose range and regimen for PTC857 that is anticipated to be

safe, well tolerated and to cause an effect in subsequent Phase 2 studies.
Part 3 * Food Effect
The secondary objective of the FE part of the study is to characterize the safety and tolerability of a single dose of PTC857 administered in healthy subjects in fed and fasted states.

Study design

This is a 3 part, single-center, randomized, double-blind, placebo-controlled, SAD, MAD, and FE study.
The study will be monitored by a Safety Review Committee (SRC). The intent of the SRC is to ensure that treatment does not pose undue risk to subjects. Safety and tolerability be assessed by the SRC between each cohort prior to ascending from one dose level to the next-higher dose level in Part 1 (SAD) and Part 2 (MAD) and prior to initiating Part 2 (MAD) and Part 3 (FE).
See CSP for details for each part.

Intervention

PTC857 is available for clinical trial use in the form of capsules (compounded) at 50 mg strength. Placebo is available as matching PTC857 for administration.

Study burden and risks

Since the study is being executed in healthy volunteers, there are no anticipated benefits of the IMP. Please see the IB for further information.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

Healthy male or female subjects aged from 18 to 55 years old, inclusive, at Screening.
Subjects must understand the nature of the study and must provide signed and dated written informed consent before the conduct of any study-related procedures.
BMI of * 19.0 kg/m2 and * 35.0 kg/m2 with a body weight * 50.0 kg for male subjects and a body weight * 45.0 kg for female subjects at Screening.
Healthy as determined by the Investigator, based upon a medical evaluation including medical history, physical examination, laboratory tests, triplicate ECG recording (average QTcF * 450 msec) and vital signs. Out of range values can be repeated once.

Exclusion criteria

History of coagulopathy.
History of fat malabsorption.
Dietary restrictions that preclude participation.
Females who are pregnant or nursing.
Subjects with a prior medical history of clinically significant gastrointestinal, renal, hepatic, neurologic, hematologic, endocrine, oncologic, pulmonary, immunologic,psychiatric, or cardiovascular disease or any other condition which, in the opinion of the Investigator, would jeopardize the safety of the subject or impact the validity of the study results.

Study design

Design

Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Placebo
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	29-06-2020
Enrollment:	82
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Nap.
Generic name:	Nap.

Ethics review

Approved WMO Date:	14-05-2020
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)

Approved WMO Date:	02-06-2020
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)

Approved WMO Date:	10-09-2020
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	15-09-2020
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
EudraCT	EUCTR2020-001328-32-NL
CCMO	NL73801.056.20

Study results

Results posted: 23-02-2022

First publication
06-12-2021